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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/525,238	10/12/2005	Marco Frentsch	GULDE-0057	7138

23599 7590 10/01/2008

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EXAMINER	
GAMBEL, PHILLIP	

ART UNIT	PAPER NUMBER
1644	

MAIL DATE	DELIVERY MODE
10/01/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/525,238	FRENTSCH ET AL.	
	Examiner	Art Unit	
	Phillip Gambel	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 July 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,9,10,13 and 14* is/are pending in the application.

4a) Of the above claim(s) *10,13 and 14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6 and 9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/22/05, 1/30/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment, filed 07/07/2008, has been entered.

Claims 1-6 and 10 have been amended.

Claims 7-8 and 11-12 have been canceled.

2. Applicant's election with traverse of Group I, directed to methods of detecting the expression of CD154, including the election of species of "methods for detection", "anti-CD40 antibody", "extracellular detection", "vital cells" and "$CD4^+$ T cells", is acknowledged.

The traversal is on the grounds that the claims relate to a single inventive concept in view of the totality of the disclosure contained in the instant specification and

That page 4, paragraph 2 of the instant specification provides ample evidence that the prior art Assenmacher's (WO 99/58977) (of record) discloses is distinct from the subject matter of the instant claims and

that it would not be an undue search burden on examining all groups.

In contrast the following of record is reiterated for applicant's convenience.
See Office Action, mailed 04/15/2008.

It is noted that Assenmacher et al. (WO 99/58977) (1449; #002) teach detecting and selecting / isolating antigen-specific T cells based upon CD154-/ CD40L-specific antibodies and employing said enriched antigen-specific T cells (see entire document, including Effector Cell Populations on pages 26-29, Cell Analysis on pages 36-39, Diagnostic Methods for Detecting Antigen-Specific T Cells on pages 39—40 and Methods of Treatment Using Enriched Antigen-Specific T Cells on pages 40-42).

Also, Berner et al. (Ann Rheum Dis 59: 190-195, 2000) (1449; #003) teach detecting and isolating antigen-specific T cells from patients with rheumatoid arthritis (See entire document, including Abstract and Conclusions on page 190; Methods, Results and Discussion).

The invention as well as the species do not provide a contribution over the prior art in that the special technical feature of employing CD154-specific/ CD40L-specific reagents / inhibitors, such as CD40L-specific antibodies have been employed in the detection and isolation of antigen-specific T cells, including their use for diagnostics and therapy. Also, Assenmacher et al. and Berner et al. teach the isolation of antigen-specific T cells, including CD154-/CD40L-expressing T cells.

Additionally, the claimed methods of detection, isolation and treatment methods rely upon different ingredients, process steps and endpoint which are not coextensive and which do not share the same technical feature

In turn, the ingredients for the methods, including the CD40/CD154 system inhibitors, differ in structure and modes of action to such an extent and require non-coextensive searches to such an extent that they are considered patentable distinct. Further, these molecules do not share a substantial structural feature essential to a common utility do not have common structure to a common utility.

Further, the diseases differ in etiologies and therapeutic endpoints.

Thus the technical feature of employing CD40L-specific reagents in detecting, isolating and using antigen-specific T cells was not special and the Groups are not so linked under PCT Rule 13.2.

Additionally, the claimed methods rely upon different ingredients, process steps and endpoint which are not coextensive and which do not share the same technical feature.

In contrast to applicant's reliance upon page 4, paragraph 2 of the instant specification that ample evidence has been provided that the prior art Assenmacher's (WO 99/58977) (1449; #002) discloses is distinct from the subject matter of the instant claims
the claims are given their broadest reasonable interpretation.

Rather than relying upon limitations not claimed,
the claimed methods of detection are readily met by the prior art references.

Further, given applicant's election of "anti-CD40 antibody" and the corresponding rejection under 35 USC 112, first paragraph, enablement herein,
the election of species has been extended to include "anti-CD40L antibodies (i.e., anti-CD154 antibodies)" in the "elected claimed methods of detection of $CD4^+$ cells" in order to advance prosecution.

Given applicant's lack of submitting evidence or identify such evidence now of record showing the species of methods of detection and methods of isolation to be obvious variants or clearly admit on the record that this is the case
Applicant's request to extend the election of species to "methods of isolation" has been denied.

Applicant request to either petition to review the Restriction Requirement or to seek reentry of any withdrawn claims once allowable subject matter has been determined is denied.

Claims 1-6 and 9 are under consideration as they read on the elected species.

Claims 13-14 have been withdrawn from consideration as being drawn to non-elected Groups or species.

3. Priority.

Receipt of the stamped WIPO foreign priority document EP 02090300.1, filed 08/23/2002, is acknowledged.

However, it does not appear that a certified English translation has not been provided in the instant application.

Therefore the effective priority date is the PCT/EP03/09354, filed 08/22/2003.

4. The following guidelines illustrate the preferred layout for the specification of a utility application. These guidelines are suggested for the applicant's use.
See MPEP 608.01(a).

Arrangement of the Specification

As provided in 37 CFR 1.77(b), the specification of a utility application should include the following sections in order. Each of the lettered items should appear in upper case, without underlining or bold type, as a section heading. If no text follows the section heading, the phrase "Not Applicable" should follow the section heading:
(a) TITLE OF THE INVENTION.
(b) CROSS-REFERENCE TO RELATED APPLICATIONS.
(c) STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT.
(d) THE NAMES OF THE PARTIES TO A JOINT RESEARCH AGREEMENT.
(e) INCORPORATION-BY-REFERENCE OF MATERIAL SUBMITTED ON A COMPACT DISC.
(f) BACKGROUND OF THE INVENTION.
(1) Field of the Invention.
(2) Description of Related Art including information disclosed under 37 CFR 1.97 and 1.98.
(g) BRIEF SUMMARY OF THE INVENTION.
(h) BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWING(S).
(i) DETAILED DESCRIPTION OF THE INVENTION.
(j) CLAIM OR CLAIMS (commencing on a separate sheet).
(k) ABSTRACT OF THE DISCLOSURE (commencing on a separate sheet).
(l) SEQUENCE LISTING. (See MPEP § 2424 and 37 CFR 1.821- 1.825. A "Sequence Listing" is required on paper if the application discloses a nucleotide or amino acid sequence as defined in 37 CFR 1.821(a) and if the required "Sequence Listing" is not submitted as an electronic document on compact disc.)

The instant specification does not provide for the correct headings, nor provides for a Brief Description of the Drawings.

In addition, applicant is invited to amend the first line of the specification to incorporate a priority line with respect to this 371 national filing of PCT/EP03/09354, filed 08/22/2003.

5. The application is required to be reviewed and all spelling, TRADEMARKS, and like errors corrected.

Trademarks should be capitalized or accompanied by the ® or ™ symbol wherever they appear and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the trademarks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Appropriate corrections are required

6. Claims 1-6 and 9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Again, as noted previously twice, the claims are subject to a rejection under 35 USC 112, second paragraph.

Claims 1-6 and 9 are indefinite under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, as they do not recite clear and definitive method steps and appear to be incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01.

Again, applicant is invited to review the claims carefully and consider amending the claims to recite positive steps and ingredients to accomplish the claimed methods.

For example, the recitation of "detecting the expression of CD154" in the absence of clear positive steps and ingredients to accomplish the claimed methods in the claims and in view of the elected species of anti-CD40 antibodies, wherein the elected methods are directed towards detecting the expression of the ligand of CD40, namely CD154/CD40 ligand/CD40L.

Also, it is noted that CD40 is not expressed extracellularly on vital $CD4^+$ T cells.

For example, the nature and parameters with respect to the recitation of "characterized" is that the nature or parameters of the claimed "characterization" is not defined by the claims and the specification does not provide a standard for ascertaining the requisite degree or direction and, in turn, one of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the invention or the parameters by which to determine said metes and bounds.

Applicant is reminded that the amendment must point to a basis in the specification so as not to add any new matter. See MPEP 714.02 and 2163.06.

7. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-6 and 9 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification disclosure is insufficient to enable one skilled in the art to practice the invention as claimed without an undue amount of experimentation. Undue experimentation must be considered in light of factors including: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill in the art, the level of predictability of the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention, see In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

With regards to the instant claims; their breadth, the state of the prior art, and the lack of guidance provided by the inventor, comprise the primary issues as regards the unpredictability of the claimed method.

As indicated above, applicant's election with traverse of Group I, directed to methods of detecting the expression of CD154, including the election of species of "methods for detection", "anti-CD40 antibody", "extracellular detection", "vital cells" and "$CD4^+$ T cells", has been acknowledged.

However, CD40 is not expressed extracellularly on vital $CD4^+$ T cell

The specification does not enable one of skill in the art, at the time the invention was made, to practice the claimed methods as currently claimed.

For example, in an effort to distinguish methods of detection from the prior art,
the instant specification describes methods of detecting antigen-specific T cells, which rely upon secretion inhibitors and endocytosis inhibitors (e.g., see page 14, paragraph 2 of the instant specification.
Here on page 14 of the specification, it is noted that the use of anti-CD40 antibodies affect CD40 in such a way that interaction with CD154 is no longer possible.

Example 3 on page 19 of the instant specification describes culturing T cells with anti-CD40 antibodies, however the detecting of CD154 is determined by anti-CD154 antibodies (i.e. anti-CD40L antibodies) antibodies and not by anti-CD40 antibodies.

It appears that the invention described in the specification as-filed relies upon stabilizing CD154 (CD40L) intracellularly in $CD4^+$ T cells with secretion inhibitors and endocytosis inhibitors as well as stabilizing CD154 with CD40-specific blocking antibodies and culture systems.

In the absence of essential ingredients and methods steps such as stabilizing CD154 (CD40L) intracellularly in $CD4^+$ T cells with secretion inhibitors and endocytosis inhibitors as well as stabilizing CD154 with CD40-specific blocking antibodies and culture systems,
there is insufficient direction and guidance as to how the disclosure enable how the skilled artisan would be able to detect the extracellular expression of CD154 on $CD4^+$ T cells with anti-CD40 antibodies.

The skilled artisan would not predict that extracellular expression of CD154 on $CD4^+$ T cells could be detected with anti-CD40 antibodies, given that anti-CD40 antibodies do not bind CD154, nor T cells.

Given the unpredictability of detecting the expression of an antigen in the absence of an agent or means to specifically detect said antigen, and lack of sufficient guidance and working examples in the present application, the experimentation left to those skilled in the art, would be unnecessarily, and improperly, extensive and undue.

As requested twice by the examiner, applicant is invited to recite clear and definitive method steps and ingredients to enable the claimed methods to detect CD154 extracellularly with anti-CD40 antibodies.

Applicant is cautioned against reading limitations into the claims and to point to a basis in the specification so as not to add any new matter.

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States

10. As indicated above, given the lack of enablement of applicant's elected species in detecting the extracellular expression of CD154 (CD40L) on $CD4^+$ T cells,
the election of species has been extended to the use of anti-CD154 (Anti-CD40L antibodies) to detect the extracellular expression of CD154 (CD40L) on $CD4^+$ T cells,

11. Claims 1-6 and 9 are rejected under 35 U.S.C. § 102(b) as being anticipated by Assenmacher et al. (WO 99/58977) (1449; #002) (see entire document).

Assenmacher et al. teach detecting antigen-specific T cells based upon CD154-/ CD40L-specific antibodies (see entire document, including Effector Cell Populations on pages 26-29, Cell Analysis on pages 36-39, Diagnostic Methods for Detecting Antigen-Specific T Cells on pages 39—40 and Methods of Treatment Using Enriched Antigen-Specific T Cells on pages 40-42).

CD154 (CD40L) is expressed on activated $CD4^+$ T cells.

Given the broadest reasonable interpretation of the claims, including detecting $CD154^+$ ($CD40L^+$) T cells from patients with an inflammatory condition,
it does not appear that the claim language or limitations result in a manipulative difference in the method steps when compared to the prior art disclosure

12. Claims 1-6 and 9 are rejected under 35 U.S.C. § 102(b) as being anticipated by Berner et al. (Ann Rheum Dis 59: 190-195, 2000) (1449; #003) (see entire document).

Berner et al. teach detecting antigen-specific T cells from patients with rheumatoid arthritis (see entire document, including Abstract and Conclusions on page 190; Methods, Results and Discussion).

CD154 (CD40L) is expressed on activated $CD4^+$ T cells.

Given the broadest reasonable interpretation of the claims, including detecting $CD154^+$ ($CD40L^+$) T cells from patients with an inflammatory condition,
it does not appear that the claim language or limitations result in a manipulative difference in the method steps when compared to the prior art disclosure

13. Claims 1-6 and 9 are rejected under 35 U.S.C. § 102(b) as being anticipated by Batataglia et al. (Am. J. Gastroenterology 94: 3279-3284, 1999) (see entire document).

Battaglia et al. teach detecting antigen-specific $CD4^+$ T cells from patients with Crohn's disease (see entire document, including Abstract, Results and Discussion).

CD154 (CD40L) is expressed on activated $CD4^+$ T cells.

Given the broadest reasonable interpretation of the claims, including detecting $CD154^+$ ($CD40L^+$) T cells from patients with an inflammatory condition,
it does not appear that the claim language or limitations result in a manipulative difference in the method steps when compared to the prior art disclosure

14. No claim is allowed.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (571) 272-0844. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eileen O'Hara can be reached on (571) 272-0878.

The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Phillip Gambel/

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September 28, 2008